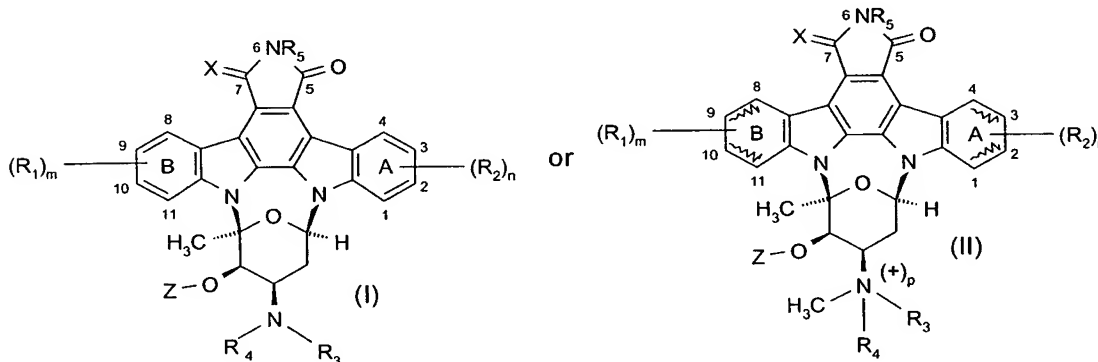


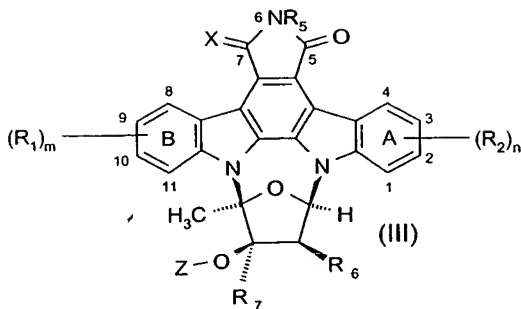
Amendments to the Claims

This listing of claims will replace all prior version, listings, of claims in the specification:

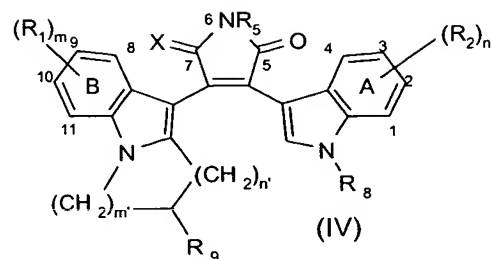
Listing of Claims:

1. (original) A method of treating myelodysplastic syndromes, lymphomas and leukemias, and solid tumors in a mammal which comprises treating the mammal in need of such treatment simultaneously, concurrently, separately or sequentially with pharmaceutically effective amounts of (a) a FLT-3 inhibitor, or a pharmaceutically acceptable salt or a prodrug thereof, and (b) a histone deacetylase inhibitor, or a pharmaceutically acceptable salt or a prodrug thereof.
2. (original) The method according to claim 1 for treating acute myeloid leukemia (AML).
3. (original) The method according to claim 1, wherein the FLT-3 inhibitor is a staurosporine derivative.
4. (original) The method according to claim 3, wherein the staurosporine derivative is selected from the compounds of formula,

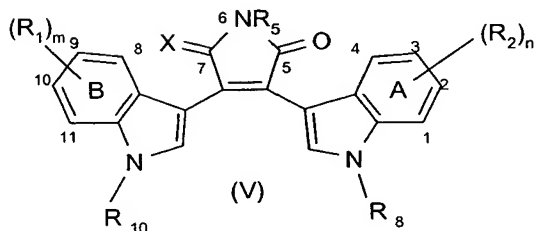




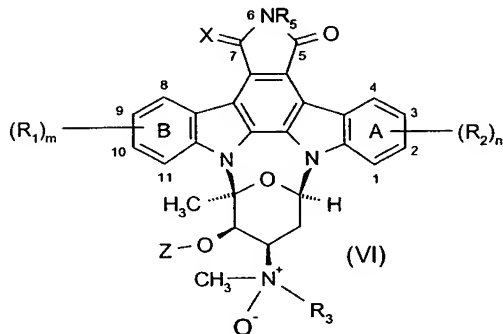
or



or



or



or

wherein R_1 and R_2 , are, independently of one another, unsubstituted or substituted alkyl, hydrogen, halogen, hydroxy, etherified or esterified hydroxy, amino, mono- or disubstituted amino, cyano, nitro, mercapto, substituted mercapto, carboxy, esterified carboxy, carbamoyl, N-mono- or N,N-di-substituted carbamoyl, sulfo, substituted sulfonyl, aminosulfonyl or N-mono- or N,N-di-substituted aminosulfonyl;

n and m are, independently of one another, a number from and including 0 to and including 4;

n' and m' are, independently of one another, a number from and including 1 to and including 4;

R_3 , R_4 , R_8 and R_{10} are, independently of one another, hydrogen, an aliphatic, carbocyclic, or carbocyclic-aliphatic radical with up to 29 carbon atoms in each case, a heterocyclic or heterocyclic-aliphatic radical with up to 20 carbon atoms in each case, and in each case up to 9 heteroatoms, an acyl with up to 30 carbon atoms, wherein R_4 may also be absent;

or R_3 is acyl with up to 30 carbon atoms and R_4 not an acyl;

p is 0 if R_4 is absent, or is 1 if R_3 and R_4 are both present and in each case are one of the aforementioned radicals;

R₅ is hydrogen, an aliphatic, carbocyclic, or carbocyclic-aliphatic radical with up to 29 carbon atoms in each case, or a heterocyclic or heterocyclic-aliphatic radical with up to 20 carbon atoms in each case, and in each case up to 9 heteroatoms, or acyl with up to 30 carbon atoms;

R₇, R₆ and R₉ are acyl or -(lower alkyl) -acyl, unsubstituted or substituted alkyl, hydrogen, halogen, hydroxy, etherified or esterified hydroxy, amino, mono- or disubstituted amino, cyano, nitro, mercapto, substituted mercapto, carboxy, carbonyl, carbonyldioxy, esterified carboxy, carbamoyl, N-mono- or N,N-di-substituted carbamoyl, sulfo, substituted sulfonyl, aminosulfonyl or N-mono- or N,N-di-substituted aminosulfonyl;

X stands for 2 hydrogen atoms; for 1 hydrogen atom and hydroxy; for O; or for hydrogen and lower alkoxy;

Z stands for hydrogen or lower alkyl;

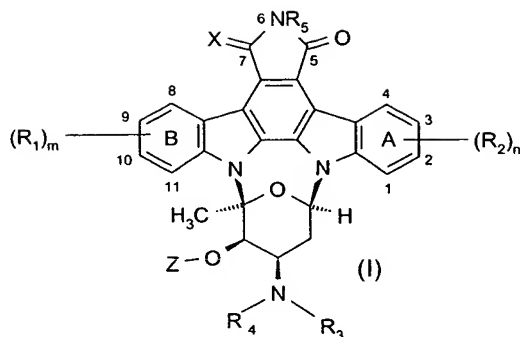
and either the two bonds characterised by wavy lines are absent in ring A and replaced by 4 hydrogen atoms, and the two wavy lines in ring B each, together with the respective parallel bond, signify a double bond;

or the two bonds characterised by wavy lines are absent in ring B and replaced by a total of 4 hydrogen atoms, and the two wavy lines in ring A each, together with the respective parallel bond, signify a double bond;

or both in ring A and in ring B all of the 4 wavy bonds are absent and are replaced by a total of 8 hydrogen atoms;

or a salt thereof, if at least one salt-forming group is present.

5. (original) The method according to claim 3, wherein the staurosporine derivative is a staurosporin derivative of formula I,



wherein

m and n are each 0;

R₃ and R₄ are independently of each other

hydrogen,

lower alkyl unsubstituted or mono- or disubstituted, especially monosubstituted, by radicals selected independently of one another from carboxy; lower alkoxycarbonyl; and cyano;

or

R₄ is hydrogen or -CH₃, and

R₃ is acyl of the subformula R^o-CO-, wherein R^o is lower alkyl; amino-lower alkyl, wherein the amino group is present in unprotected form or is protected by lower alkoxycarbonyl;

tetrahydropyranyloxy-lower alkyl; phenyl; imidazolyl-lower alkoxyphenyl; carboxyphenyl; lower alkoxycarbonylphenyl; halogen-lower alkylphenyl; imidazol-1-ylphenyl; pyrrolidino-lower alkylphenyl; piperazino-lower alkylphenyl; (4-lower alkylpiperazinomethyl)phenyl; morpholino-lower alkylphenyl; piperazinocarbonylphenyl; or (4-lower alkylpiperazino)phenyl;

or is acyl of the subformula R^o-O-CO-, wherein R^o is lower alkyl;

or is acyl of the subformula R^oHN-C(=W)-, wherein W is oxygen and R^o has the following meanings: morpholino-lower alkyl, phenyl, lower alkoxyphenyl, carboxyphenyl, or lower alkoxy-carbonylphenyl;

or R₃ is lower alkylphenylsulfonyl, typically 4-toluenesulfonyl;

R₅ is hydrogen or lower alkyl,

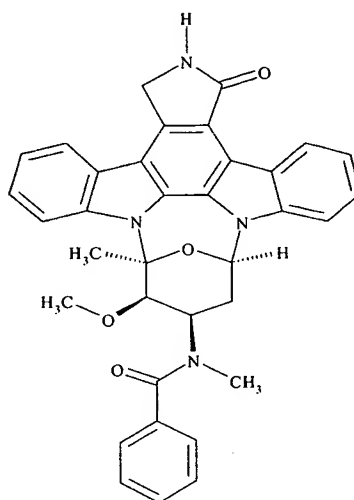
X stands for 2 hydrogen atoms or for O;

Z is methyl or hydrogen;

or a salt thereof, if at least one salt-forming group is present.

6. (original) The method according to claim 3, wherein the staurosporine derivative is *N*-[(9*S*,10*R*,11*R*,13*R*)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1*H*,9*H*-

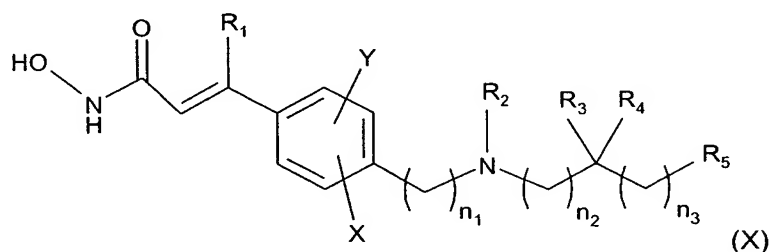
diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-*N*-methylbenzamide of the formula (VII):



(VII)

or a salt thereof.

7. (original) The method according to claim 1, wherein the HDAl compound is a histone deacetylase inhibitor of formula (X)



(X)

wherein

R_1 is H, halo, or a straight chain C_1 - C_6 alkyl;

R_2 is selected from H, C_1 - C_{10} alkyl, C_4 - C_9 cycloalkyl, C_4 - C_9 heterocycloalkyl, C_4 - C_9 heterocycloalkylalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, $-(CH_2)_nC(O)R_6$, $-(CH_2)_nOC(O)R_6$, amino acyl, $HON-C(O)-CH=C(R_1)$ -aryl-alkyl- and $-(CH_2)_nR_7$;

R_3 and R_4 are the same or different and independently H, C_1 - C_6 alkyl, acyl or acylamino, or R_3 and R_4 together with the carbon to which they are bound represent $C=O$, $C=S$, or $C=NR_8$, or R_2 together with the nitrogen to which it is bound and R_3 together with the carbon to which it is bound can form a C_4 - C_9 heterocycloalkyl, a heteroaryl, a

polyheteroaryl, a non-aromatic polyheterocycle, or a mixed aryl and non-aryl polyheterocycle ring;

R₅ is selected from H, C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, acyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, aromatic polycycle, non-aromatic polycycle, mixed aryl and non-aryl polycycle, polyheteroaryl, non-aromatic polyheterocycle, and mixed aryl and non-aryl polyheterocycle;

n, n₁, n₂ and n₃ are the same or different and independently selected from 0 - 6, when n₁ is 1-6, each carbon atom can be optionally and independently substituted with R₃ and/or R₄;

X and Y are the same or different and independently selected from H, halo, C₁-C₄ alkyl, NO₂, C(O)R₁, OR₉, SR₉, CN, and NR₁₀R₁₁;

R₆ is selected from H, C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, OR₁₂, and NR₁₃R₁₄;

R₇ is selected from OR₁₅, SR₁₅, S(O)R₁₆, SO₂R₁₇, NR₁₃R₁₄, and NR₁₂SO₂R₆;

R₈ is selected from H, OR₁₅, NR₁₃R₁₄, C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R₉ is selected from C₁ - C₄ alkyl and C(O)-alkyl;

R₁₀ and R₁₁ are the same or different and independently selected from H, C₁-C₄ alkyl, and - C(O)-alkyl;

R₁₂ is selected from H, C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, C₄ - C₉ heterocycloalkylalkyl, aryl, mixed aryl and non-aryl polycycle, heteroaryl, arylalkyl, and heteroarylalkyl;

R₁₃ and R₁₄ are the same or different and independently selected from H, C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, amino acyl, or R₁₃ and R₁₄ together with the nitrogen to which they are bound are C₄ - C₉ heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle;

R₁₅ is selected from H, C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl and (CH₂)_mZR₁₂;

R₁₆ is selected from C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, aryl, heteroaryl, polyheteroaryl, arylalkyl, heteroarylalkyl and (CH₂)_mZR₁₂;

R₁₇ is selected from C₁-C₆ alkyl, C₄ - C₉ cycloalkyl, C₄ - C₉ heterocycloalkyl, aryl, aromatic polycycle, heteroaryl, arylalkyl, heteroarylalkyl, polyheteroaryl and NR₁₃R₁₄;

m is an integer selected from 0 to 6; and

Z is selected from O, NR₁₃, S and S(O);

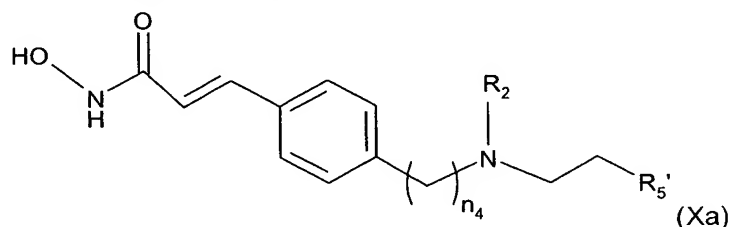
or a pharmaceutically acceptable salt thereof.

8. (original) The method according to claim 7, wherein each of R₁, X, Y, R₃, and R₄ is H.

9. (original) The method according to claim 8, wherein one of n_2 and n_3 is zero and the other is 1.

10. (original) The method according to claim 9, wherein one of n_2 and n_3 is zero and the other is 1.

11. (original) The method according to claim 1, wherein the histone deacetylase inhibitor is a compound of the formula (Xa)



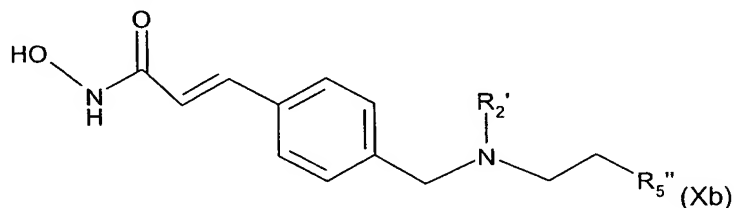
wherein

n_4 is 0-3,

R_2 is selected from H, C_1 - C_6 alkyl, C_4 - C_9 cycloalkyl, C_4 - C_9 heterocycloalkyl, alkylcycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, $-(CH_2)_nC(O)R_6$, amino acyl and $-(CH_2)_nR_7$;

R_5' is heteroaryl, heteroarylalkyl, an aromatic polycycle, a non-aromatic polycycle, a mixed aryl and non-aryl polycycle, polyheteroaryl, or a mixed aryl and non-aryl polyheterocycle or a pharmaceutically acceptable salt thereof.

12. (original) The method according to claim 1, wherein the histone deacetylase inhibitor is a compound of the formula (Xb):



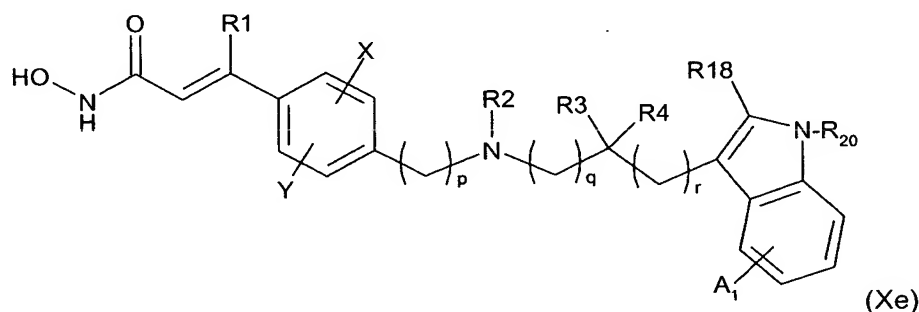
wherein

R_2' is selected from H, C_1 - C_6 alkyl, C_4 - C_6 cycloalkyl, alkylcycloalkyl, and $(CH_2)_{2-4}OR_{21}$ where R_{21} is H, methyl, ethyl, propyl, or isopropyl, and

R_5'' is unsubstituted or substituted 1*H*-indol-3-yl, benzofuran-3-yl or quinolin-3-yl or a pharmaceutically acceptable salt thereof.

13. (original) The method according to claim 1, wherein the histone deacetylase inhibitor is a compound of the formula

(Xe)



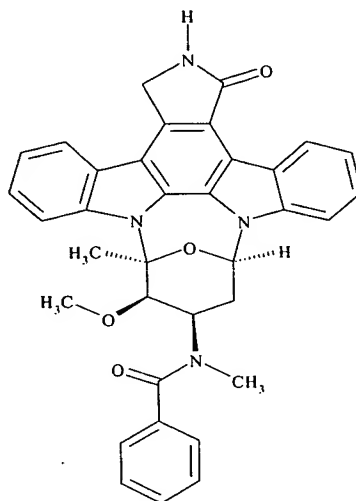
or a pharmaceutically acceptable salt thereof.

14. (currently amended) The method according to any one of ~~claims 1 to 6~~ claim 1, wherein the histone deacetylase inhibitor is selected from the group consisting of N-hydroxy-3-[4-[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propenamide, or, in each case a pharmaceutically acceptable salt thereof.

15. (original) Use of a combination of (a) a FLT-3 inhibitor and (b) a histone deacetylase inhibitor (HDAI) for treating myelodysplastic syndromes, lymphomas and leukemias, and solid tumors.

16. (original) Use according to claim 15 for treating acute myeloid leukemia (AML), colorectal cancer (CRC) or non-small cell lung cancer (NSCLC).

17. (original) Use according to claim 15, wherein the FLT-3 inhibitor is -[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-N-methylbenzamide of the formula (VII):



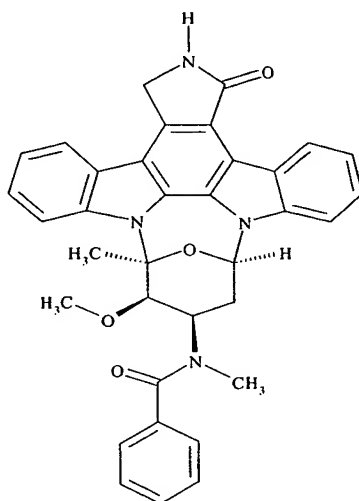
(VII)

or a salt thereof and the HDAl is selected from the group consisting of N-hydroxy-3-[4-[[[2-hydroxyethyl][2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propenamide, or, in each case a pharmaceutically acceptable salt thereof.

18. (original) Use of a combination of (a) a FLT-3 inhibitor and (b) a histone deacetylase inhibitor (HDAl) for the preparation of a medicament for the treatment of myelodysplastic syndromes, lymphomas and leukemias and solid tumors.

19. (original) Use according to claim 18 for treating acute myeloid leukemia (AML), colorectal cancer (CRC) or non-small cell lung cancer (NSCLC).

20. (original) Use according to claim 18, wherein the FLT-3 inhibitor is -[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-N-methylbenzamide of the formula (VII):



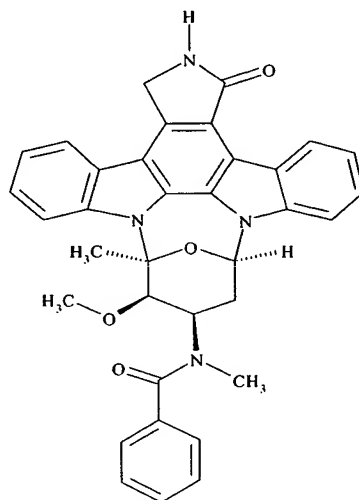
(VII)

or a salt thereof and the HDAI is selected from the group consisting of N-hydroxy-3-[4-[[[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propenamide, or, in each case a pharmaceutically acceptable salt thereof.

21. (original) A pharmaceutical composition comprising (a) a FLT-3 inhibitor and (b) a histone deacetylase inhibitor for the treatment of myelodysplastic syndromes, lymphomas and leukemias and solid tumors.

22. (original) A pharmaceutical composition according to claim 21 for treating acute myeloid leukemia (AML), colorectal cancer (CRC) or non-small cell lung cancer (NSCLC).

23. (original) A pharmaceutical composition according to claim 21, wherein the FLT-3 inhibitor is -[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-N-methylbenzamide of the formula (VII):



(VII)

or a salt thereof and the HDAI is selected from the group consisting of N-hydroxy-3-[4-[[[2-hydroxyethyl][2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide, N-hydroxy-3-[4-[[[2-(1H-indol-3-yl)ethyl]-amino]methyl]phenyl]-2E-2-propenamide and N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2E-2-propenamide, or, in each case a pharmaceutically acceptable salt thereof.